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CONTENTS

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INDONESIAN JOURNAL OF
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CASE REPORT

A THIRTY-ONE-YEARS-OLD FEMALE WITH SLE AND SYSTEMIC SCLERODERMA

(Perempuan Usia 31 Tahun dengan SLE dan Skleroderma Sistemik)

Rahardjo, Rachmawati

ABSTRAK

Systemic Lupus Erythematosus (SLE) adalah penyakit rematik autoimun yang ditandai adanya inflamasi luas, yang mempengaruhi setiap organ atau sistem dalam tubuh. Sklerosis sistemik (skleroderma) adalah penyakit multisistem kronis yang tidak diketahui penyebabnya, ditandai dengan penebalan kulit akibat penumpukan jaringan ikat disertai kelainan fungsi dan bentuk organ visceral. Seorang perempuan 31 tahun mengalami nyeri jari-jari dan sendi. Lima tahun lalu didiagnosis kusta serta diobati selama satu tahun. Pemeriksaan fisik didapatkan mouse face appearance, teleangiektasis, salt and pepper appearance, sclerodactili, artritis, serta calcinosis. Peregangan dan pengerasan kulit simetris. Hemoglobin menurun, sediaan darah tepi terdapat sebaran roleaux, neutrofilia dan limfosit teraktivasi. Indirect Coomb Test (ICT) inkompatibel. SGOT, total protein, globulin meningkat. Anti Ds-DNA meningkat lima kali dan ANA meningkat dua puluh kali lipat dari batas normal. Diagnosis SLE didasarkan pada peningkatan kadar ANA dan Ds-DNA. Skleroderma didasarkan pada pemeriksaan fisik, pemeriksaan hematologi dan anti Scl-70 (anti tropoisomerase I)

Kata kunci: *Systemic lupus erythematosus, skleroderma, ANA, Ds-DNA, anti Scl-70*

ABSTRACT

Systemic Lupus Erythematosus (SLE) is an autoimmune rheumatic disease characterized by widespread inflammation affecting each organ or system in the body. Systemic sclerosis (scleroderma) is a chronic multisystem disease of unknown cause, characterized by thickened skin with connective tissue dysfunction and forms of visceral organs A 31-year old female felt pain in the fingers and joints. Five years ago she was diagnosed with leprosy and was medicated for a year. On physical examination a mouse face appearance, teleangiektasis, salt and pepper appearance, sclerodactili, arthritis and calcinosis was found. Symetrical stretching and hardening of the skin was also found. Hemoglobin was decreased, roleaux, neutrophilia and activated lymphocytes were found. Indirect Coombs Test (ICT) was incompatible. Alanine transaminase (ALT), total protein, globulin were increased. Increasing Anti-ds-DNA five times and ANA twenty times the normal limit was also found. The diagnosis of SLE was based on increasing levels of ANA and ds-DNA. Scleroderma was based on physical examination, hematological examination and anti-Scl-70 (anti tropoisomerase I).

Key words: Systemic lupus erythematosus, scleroderma, ANA, Ds-DNA, anti Scl-70

INTRODUCTION

Systemic Lupus Erythematosus ((SLE) is an autoimmune rheumatic disease characterized by widespread inflammation, affecting each organ or system in the body. The disease is associated with deposition of autoantibodies and immune complexes, causing tissue damage.[1]

Systemic sclerosis (scleroderma) is a chronic multisystem disease of unknown cause, characterized by thickening of the skin due to accumulated connective tissue (connective), accompanied by abnormalities in the function and form of the visceral organs including the gastrointestinal tract, lungs, heart and kidneys.[2] The prevalence of scleroderma is relatively low, children and young adults are rarely

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affected. Age 30–50 years are most affected by this disease. Females risk are 3 times more than males. The pathogenesis scleroderma is very complex, suspected as a trigger factor but until now has not known for certain.[2,3]

CASE REPORT

A 31-year old female came to the Dr. Kariadi General Hospital (RSDK) Semarang on January 1, 2015 due to pain fingers and heavy joints which caused difficulty of walking since the last two weeks. From autoanamnesis, the following data were obtained: October 2014, the patient was treated in Brebes Hospital because of pain throughout the body, shortness of breath and chest pain and was diagnosed with scleroderma, multiple sclerosis, treated for 4 days, home improvement. Then the pain in the fingers and joints, advanced since the last two weeks and it was hard for her to walk so she was brought to the Dr. Kariadi Hospital.

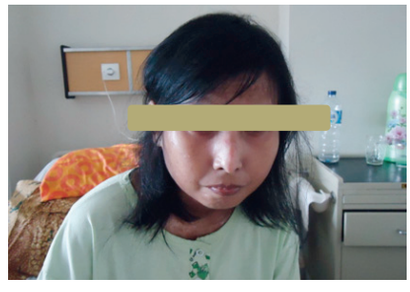
Four years ago the patient felt stiffeness of the whole body, from arms spreading throughout the body, pain in the fingers and joints, advanced since the last 2 weeks, difficulties of walking so she was brought to the Dr. Kariadi Hospital. Darkened skin appearence, difficulty of swallowing, relapsing and remitting, shortness of breath, cough with phlegm, irregular menstruation, no redness of skin when exposed to sunlight, no fever, weight loss, bowel and bladder as usual.

In 2010 patient suffered from black spots on the body and was diagnosed with leprosy, taking medication of MDT for 1 year at the health center until otherwise recovered. In 2011 she experinced stabbing pain of skin and stiffness making it difficult to walk. In the year 2012 she was stiff all over the body. In 2013, while pregnant, index finger and middle finger of the right and left hands were stiff and could not be bent. After delivery, the fingers began to bend, but could not be straightened/moved, this spread throughout the body and experienced difficulty in walking.

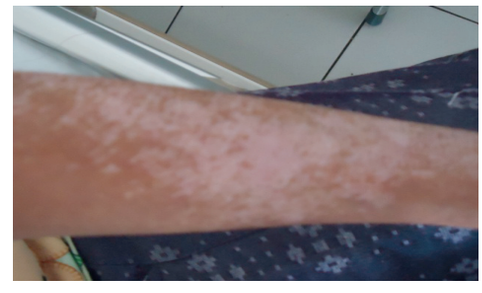
There were no family members with similar diseases, a history of drug or food allergies.

Physical examination

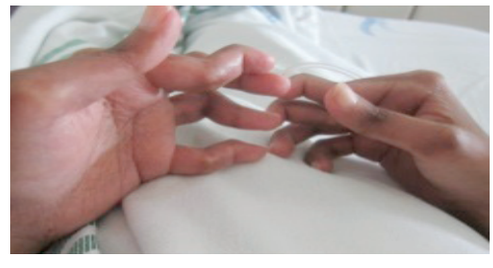
Physical examination showed a good general condition, the impression of malnutrition with weight 40 kg, height 156 cm and anthropometric including underweight with thin stature, her face looked like mouse face appearance. Blood pressure 130/70 mm Hg, pulse 88 ×/minute, respiratory rate 20 ×/min and axillary temperature of 36.5°C. No abnormalities in the eyes, mouth and neck were found. The nose looked teleangiektasis. There were no abnormalities on examination of the heart, lungs and abdomen. Extremities showed salt and pepper appearance, sclerodactili, arthritis, calcinosis and Raynaud's phenomenon. There was thickening, hardening of the skin stretching and symmetrical.



Mouse face appearance



Salt and pepper appearance



Sclerodactili

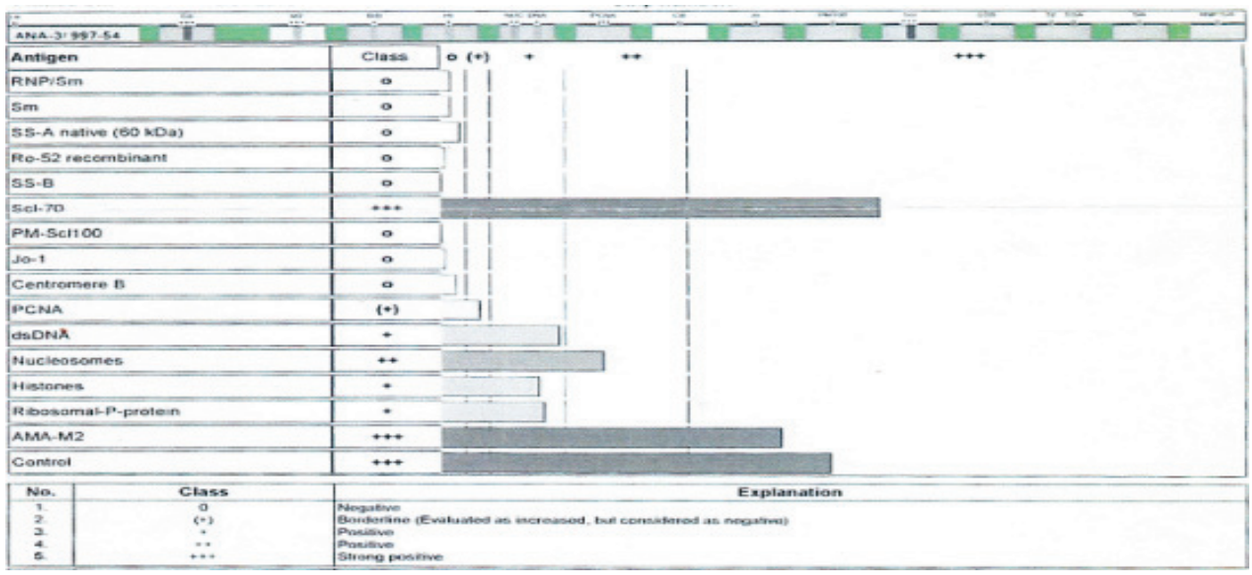
LABORATORY EXAMINATION

Hematological examination, showed a decrease in hemoglobin. Peripheral blood picture showed spread roleaux, neutrophilia and activated lymphocytes. Indirect Coombs Test (ICT) was incompatible and Direct Coombs Test (DCT) +3 resulted that a blood transfusion could not be done. Clinical chemistry examination showed a decrease in urea and increased creatinine, sodium and chloride and potassium within normal limits. Alanine Transaminase (ALT) and AST increased. Increased total protein, albumin within normal limits, globulin increased. Anti ds-DNA increased fivefold and Anti Nuclear Antibodies (ANA) increased twenty times the normal limit. Urinalisis examination was within normal limits. Test results showed Reitz negative serum. The results of radiological examination X-obliq AP manus photo illustration showed calsinosis which seemed to be supportive of the sclerodactili manus dextra et sinistra. Oesophagus Maag Duodenum (OMD) (esophagus, duodenum ulcer) result showed their luminal narrowing at the third distal of the esophagus as high as V Th 10–12 with contrasting passages slowed in the segment, which was visible on fluoroscopy examination.

Table 1. Laboratory examination

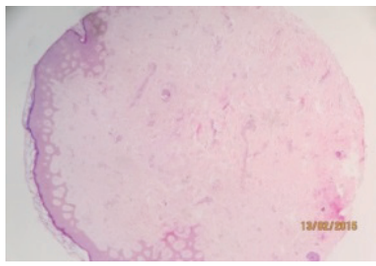
	01/01/2015	08/01/2015	20/01/2015	Normal range/unit
Hemoglobin	8.8	12.4	12.3	12.0–15.0 g%
Hematocrite	25.3	38.3	36.9	35.0–47.0%
Erythrocytes	3.1	4.48	4.4	3.90–5.60 106/μL
MCH	28.5	27.7	27.8	27.0–32.0 pg
MCV	82.4	85.4	83.6	76.0–96.0 fl
MCHC	31.60	32.4	33.3	29.0–36.0 g/dL
Leucocyte	5.8	6.51	12.7	4–11 103/μL
Platelets	352.8	358	420	150–400 103/μL
Blood sugar	115			80–160 mg/dL
Ureum	8			15–39 mg/dL
Creatinin	0.30			0.6–1.3 mg/dL
Sodium	143			136–145 mmol/L
Potassium	4.0			3.5–5.1 mmol/L
Chloride	106			98–107 mmol/L
AST	46			15–34 U/L
ALT	39			15–60 U/L
Total protein	9.7			6.4–8.2 g/dL
Albumin	3.3			3.4–5.0 g/dL
Globulin	6.4			2.3–3.5 g/dL
ESR 1 hour		76	61	3–14/hours
ESR 2 hour		90	81	
Test	**Result**	**Unit**		**Normal range**
Anti Ds DNA	1193.0	IU/mL		Negative 0–200
				Equivocal 201–300
				Positive >300
ANA	137.1	Unit		Negative <20
				Equivocal 20–60
				Positive >60
CRP qualitative	+/positive			

Other Test
ANA Profiles:

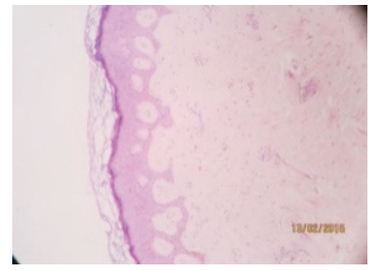


Anti Scl-70 +++ (strong positive)

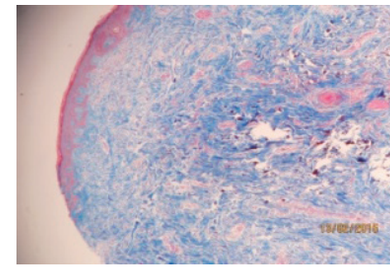
Skin biopsy:



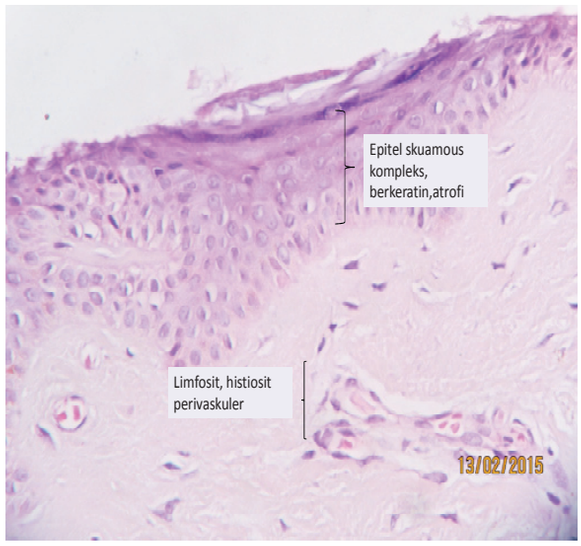
Magnifying 40×:
coated complex keratinized
squamous epitehelium, atrophy



Magnification 100×



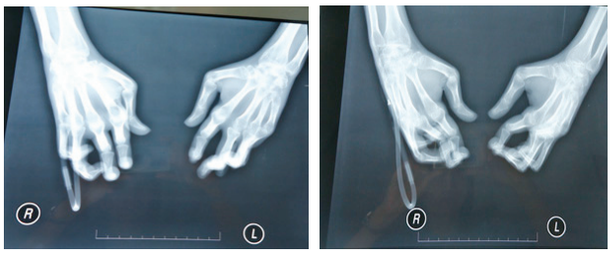
Trichrome stain:
Blue stained connective tissue



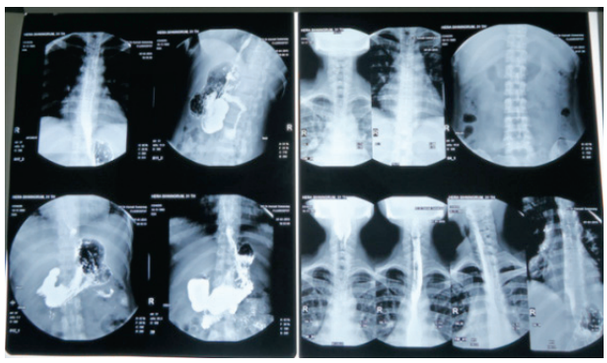
Skin biopsy of volar antebrachii dextra.

Conclusion: sign of scleroderma

Manus AP-Obliq X-Ray



OMD (Oesophagus Maag Duodenum)
X-Ray



Narrowing of the lumen in the distal third of the esophagus as high as 10–12 thoracic vertebrae with contrasting passages which slowed in the segment, which was visible on fluoroscopy examination

SCLERODERMA CRITERIA

Criteria	
Major: Thickening, hardening of the skin stretching and symmetrical metacarpophalangeal or metatarsophalangeal joints. Can involve all of the extremities, face, neck and torso (chest and abdomen)	(+)
Minor: • Sclerodactyly: skin changes as mentioned above, but only on the fingers. • Sunken fingers or lost of substance fingers. The area which was sunken was on the fingertip or the loss of the substance of the finger caused by ischemia. • Basal pulmonary fibrosis. Linear or lineonodular overview which was retibular, especially in the second basal lung looks at the picture of standard chest photo. Overview lungs may cause patches of diffuse or honeycomb, is not a primary lung disorder	 (+) (+) (–)

SLE criteria according to the *American College of Rheumatology* (ACR)

ACR-SLE criteria	Positive/Negative
Malar rash	(–)
Discoid lession	(–)
Photosensitivity	(–)
Mouth ulceration	(–)
Arthritis	(+)
Serositis	(–)
Kidney disorders	(–)
Neurological disorders	(–)
Hematological disorders	(+)
Immunological disorders (ds DNA)	(+)
Anti Nuclear Antibodies (ANA)	(+)
Score	4

Clinical diagnosis:

Systemic Lupus Erythematosus (SLE) and Systemic Scleroderma.

Treatment:

Fluid therapy was given in the form of 20 drops RL per minute, improved nutrition with regular 1700 calory diet, corticosteroid-0-4mg, metilprednisolone 16 mg orally, azathioprine 25 mg per 12 hours on the third day and given omeprazole 20 mg per 12 hours and domperidone 10 mg per 12 hours orally.

DISCUSSION

The SLE, patient initially experience black spots on the skin five years ago and given medications leprosy. In the inspection of other diseases like leprosy, presence or absence of anesthesia will very much help the diagnosis, although it is not always clear. Later on came the pain and stiffness that was advancing accompanied by abnormalities in the joints of the fingers and toes. Manifestation of SLE is so diverse that it often goes unrecognized because the clinical manifestations often do not occur simultaneously. The clinical features of the joint or musculoskeletal involvement is found in 90% of cases, although arthritis as an early manifestation is only found in 55% of cases.[4] This patient only complained of joint pain.

Pathophysiology is definitely still elusive. Systemic lupus erythematosus is characterized by the presence of autoantibody production, immune complex formation and episodes of uncontrolled complement activation and is caused by the interaction between genes and environmental factors playing a role suspected to produce abnormal immune responses.[14]

Giving leprosy drugs can stimulate the onset of SLE for induction such as minocycline and rifampicin. Pathophysiology of Drug-Induced Lupus erythematosus (DIL) is not yet fully known. Predisposing factors are drugs which decreased the body metabolic rate significantly in patients with a deficiency of the enzyme N-acetyltransferase. DIL patients show elevated levels of hydralazine formed when leukocyte are activated and an increase in free radicals and oxidants reaction. It reacts with the oxidant to form the reactive species so hydralazine binds to the protein.[15]

If the 4 or more American College of Rheumatology criteria are found, a diagnosis of SLE had a sensitivity of 85% and specificity of 95%. When only three criteria and one of them is a positive ANA, it is very likely SLE and diagnosis is based on clinical observations. When the results of the ANA test are negative then there are other possibilities instead of SLE. If only positive ANA test and other clinical manifestations do not exist is not necessarily SLE and long-term observation is required.[11] This patient shows 5 of 11 ACR criterias which has positive ANA and negative ds-DNA, so the diagnosis of SLE can be enforced.

Anti Nuclear Antibodies (ANA) test is usually used as a screening test. Unknown, 95% of patients with SLE have positive ANA test results. If the patient shows symptoms of SLE but negative ANA test, usually there is a strong enough evidence for the diagnosis of SLE. When a positive ANA test, it does not mean a person has lupus. The positive result is only an indicator, not diagnostic. This situation can be found in other diseases such as rheumatoid arthritis, Sjogren's syndrome, scleroderma, infectious diseases (malaria, subacute bacterial endocarditis, mononucleosis, autoimmune thyroid disease).[4]

Raynauld phenomenon, arthritis and sclerodactyly is common in overlapping syndrome, when encountering serious manifestations of polymyositis and alveolar fibrosis.[5]

Prognosis in SLE varies depending on the complications and severity of disease. With good control at the initial acute phase, prognosis can be good.[16]

Systemic sclerosis (scleroderma) is a chronic multisystem disease of unknown cause, characterized by thickened skin due to accumulated connective tissue (connective), accompanied by abnormalities in the function and form of the visceral organs including the gastrointestinal tract, lungs, heart and kidneys.[6]

Diagnosis is based on history and physical examination, investigation is a supporting and assisting in predicting prognosis.[8] There are five common clinical manifestations abbreviated Calcinosis, Raynaud's phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasia (CREST) can appear in whole or in part. Calsinosis is the formation of calcium deposits in tissues (can occur under the skin of the finger, arm, leg and knee, causing pain and infection when it penetrates into the surface of the skin). Raynaud's phenomenon is a localized vasoconstriction in the fingers and extremities. Esophageal dysmotility is malfunctioning esophageal spontaneous movement. Sclerodactyly is a hardening of the skin of the fingers, while telangiectasia is an abnormal dilatation of capillaries and small arteries that often form angioma (in the form of swelling or tumor).[9] This patient showed calsinosis, Raynaud's phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasia.

Laboratory tests are needed to support the diagnosis, monitoring and prognosis. Examination of the Erythrocyte Sedimentation Rate (ESR), C-reactive

protein increased. Anemia can be caused by chronic disease, iron deficiency due to gastrointestinal bleeding, a deficiency of vitamin B12 and folic acid deficiency.[5,8] This patient mild anemia was found and increased ESR but cardiac echocardiographic examination showed no abnormalities.

Specific autoantibodies for scleroderma are anti Scl-70 and anticentromer.[1,6] Anti Scl-70 was found in the comparison group (control) healthy persons, patients with Connective Tissue Disease (CTD) or in other primary Raynaud's phenomenon, so it is used to confirm a clinical diagnosis of systemic sclerosis. Antitopoisomerase I (Scl-70) is an antibody to the enzyme component of DNA topoisomerase I. This antibody is generally associated with skin changes, fibrosis of the heart, lungs and scar tissue in patients with scleroderma fingers. Anticentromer antibodies and antibody simultaneously Scl-70 is important for patients with scleroderma. Scl-70 is associated with diffuse disease and bad prognosis, whereas anticentromer associated with limited skin involvement and provide a better prognosis, though sometimes overlapping.[4,7]

The prognosis is mostly good for patients with scleroderma in a restricted area on the skin that do not undergo pulmonary complications. The prognosis is worse for diffuse skin disease, especially at an older age and for men. Death occurs most often from complications of the heart, lungs and kidneys. In diffuse skin disease, 5-year survival was 70%, 10-year survival were 55%.[16]

CONCLUSION AND SUGGESTION

According to history, physical examination and investigations, the diagnosis of SLE and systemic scleroderma can be established. Multi-Slice Computer Tomography (MSCT) of Thorax is done to see if pulmonary fibrosis is show.

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